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L40	L39 and l35	11	L40
L39	non-aspirin or non aspirin or non-steroidal or non steroidal	16054	L39
L38	L37 and l35	8	L38
L37	rofecoxib or nabumetone or apazone or nimensulide or indomethacin or sulindac or etodolac	16683	L37
L36	l26 and l35	10	L36
L35	l5 or l29	242	L35
L34	l29 and l32	5	L34
L33	l29 same l32	0	L33
L32	naproxen or sodium daproxen or fenoproxen or ketoproxen or fluurbioprofen or oxaprozin or piroxicam or meloxicam or tenoxicam or ampiroxicam or droxicam or pivoxicam or phenylbutazone or oxyphenbutazone or antipyrine or aminopyrine or dipyrine or celecoxib	15991	L32
L31	l8 same l29	5	L31
L30	L29 same l26	3	L30

L29	isoalpha acid or iso-alpha acid or iso alpha acid	240	L29
L28	iso-alpha acid or isoalpha cid or iso alpha acid	209	L28
L27	l26 same l6	0	L27
L26	salicyclic acid or methyl salicylate or difulunisal or salsalate or olsalazine or sulfasalazine or acetanilide or acetanilide or acetaminophen or phenacetin or mefenamic acid or sodium meclofenamate or tolmetin or ketoorolac or diclofenac or ibuprofen	43174	L26
L25	l8 same l1	147	L25
L24	l8 and l1	1509	L24
L23	l8 and l1	1509	L23
L22	L21 and l6	7	L22
L21	ibuprofen	13883	L21
L20	l19 and l8	6	L20
L19	spent hops	141	L19
L18	l10 same l1	6	L18
L17	l10 and l1	123	L17
L16	l8 and l15	23	L16
L15	L14 same l13	1255	L15
L14	boil$6	683508	L14
L13	hops	39768	L13
L12	l6 and l10	1	L12
L11	L10 and l8	6664	L11
L10	naproxen	8316	L10
L9	l6 and l8	10	L9
L8	anti-inflammatory or pain or antiinflmmatory or anti inflmmatory	164239	L8
L7	L6 same l2	2	L7
L6	l4 or l5	69	L6
L5	dihydro-isohumulone or dihydro-isocohumulone or dihydro-adhumulone	10	L5
L4	isoalpha acid	65	L4
L3	l1 same l2	48	L3
L2	anti-inflammatory	63944	L2
L1	beer	59387	L1

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NEWS 14	OCT 27	DIOGENES content streamlined
NEWS 15	OCT 27	EPFULL enhanced with additional content

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=> s (iso-alpha acid?) or (isoalpha acid?)
L1 432 (ISO-ALPHA ACID?) OR (ISOALPHA ACID?)

=> s anti-inflammatory or antiinflmmatory or anti-inflmmatory or pain?
L2 732900 ANTI-INFLAMMATORY OR ANTIINFLMMATORY OR ANTI-INFLMMATORY OR PAIN?

=> s l1 and l2
L3 8 L1 AND L2

=> d 1-8 ab,bib

L3 ANSWER 1 OF 8 CA COPYRIGHT 2005 ACS on STN
AB The invention provides a composition comprising a reduced **isoalpha acid** (RIAA), selected from dihydroisohumulone, dihydroisocohumulone and dihydroadhumulone, and **isoalpha acid** (IAA), selected from isohumulone, isocohumulone, and isoadhumulone, isolated from hops, wherein the RIAA and IAA are in a ratio of about 3:1 to about 1:10. The invention also provides a method of reducing inflammation by administering a composition comprising a reduced **isoalpha acid** (RIAA) and **isoalpha acid** (IAA) isolated from hops, wherein the RIAA and IAA are in a ratio of about 3:1 to about 1:10. For example, synergy of PGE2 inhibition produced by four combinations of RIAA and IAA (3:1, 3:2, 1:1 and 1:10, resp.) was demonstrated in Raw 264.7 cells. Particularly relevant synergy occurred at the 1:1 and 1:10 RIAA/IAA ratios, at RIAA concns. <0.58 μg/mL and RIAA concns. >0.31 μg/mL.
AN 143:253900 CA
TI Synergistic **anti-inflammatory** compositions comprising an **isoalpha acid** and a reduced **isoalpha acid** from hops
IN Babish, John G.; Tripp, Matthew L.; Bland, Jeffrey S.
PA USA
SO U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005192356	A1	20050901	US 2004-789814	20040227
	WO 2005084680	A1	20050915	WO 2005-US6216	20050226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-789814 A 20040227

L3 ANSWER 2 OF 8 CA COPYRIGHT 2005 ACS on STN
AB A key component of inflammation is the increase in prostaglandin biosynthesis resulting from induction of the cyclooxygenase 2 (COX2) gene. The COX2 enzyme is the prime target of non-steroidal **anti-inflammatory** drug (NSAID) therapy. COX2 is constitutively expressed in some tissues such as the gastrointestinal tract and its inhibition may result in GI toxicity. Our goal was to identify inhibitors

of prostaglandin production that were not direct COX enzyme inhibitors. We screened natural products for inhibition of prostaglandin E2 production in lipopolysaccharide (LPS)-induced mouse macrophage RAW 264.7 cells. Altering the test, methodol. allowed circumstantial assessment of in vitro inhibition of COX1 and COX2 enzymes, or COX2 gene induction. Various hop (hydrophobic and hydrophilic) and modified (IAA, RIAA, THIAA, HHIAA) hop exts. were found to be among the most potent PGE2 inhibitors in LPS induced (PGE2 from COX2) but not non-induced (PGE2 from COX1) RAW 264.7 cells, indicating COX2 selectivity (ranging from 1.5- to 363-fold). In a human gastric mucosal cell (AGS) model where COX2 is constitutively expressed, a CO2 hop extract showed strong inhibition of PGE2; in contrast, no significant PGE2 inhibition was observed by the other hop exts., indicating a lack of direct COX enzyme inhibition. Correlating the in vitro models [log10 (IC50AGS/IC50 RAW264.7)] allowed us to calculate a therapeutic index for each hop extract compared to various NSAIDs. We conclude that RIAA, IAA, THIAA, HHIAA, BA, and AA have strong potential as **anti-inflammatory** agents and predict, from our models, that they may have a low GI toxicity. An RIAA based **anti-inflammatory** preparation, Meta050, was tested clin. in a human pilot trial and showed efficacy against osteoarthritis **pain**.

AN 143:186388 CA

TI Hop and modified hop extracts have potent in vitro **anti-inflammatory** properties

AU Tripp, M.; Darland, G.; Lerman, R.; Lukaczer, D.; Bland, J.; Babish, J.

CS Metagenics Research and Development, Gig Harbor, WA, 98332, USA

SO Acta Horticulturae (2005), 668(Proceedings of the 1st International Humulus Symposium, 2004), 217-227
CODEN: AHORA2; ISSN: 0567-7572

PB International Society for Horticultural Science

DT Journal

LA English

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 CA COPYRIGHT 2005 ACS on STN

AB The invention provides hops (Humulus lupulus) exts. or derivs. thereof, such as humulone, cohumulone, adhumulone, isohumulone, etc., for use in treating a patient prophylactically and/or therapeutically for ulcerogenic-type disorders of the stomach and/or intestines. The ulcerogenic disorders can be induced chemical, environmentally, by infection, and/or by stress. The invention also provides a pharmaceutical composition comprising an active amount of hops exts. or derivs. thereof, in combination with an analgesic compound and/or an **anti-inflammatory** compound The invention further provides for use of hops exts. or derivs. thereof, significantly reducing and/or therapeutically treating ulcerogenic-type disorders of the stomach and/or intestines. For example, the hop preparation Redihop containing rho-**iso**-.**alpha**.-**acids** when combined with NSAIDs (ibuprofen and aspirin) not only attenuated the gastropathy of NSAIDs by decreasing an inhibition of PGE2 synthesis in AGS human gastric mucosal cells, but also increased therapeutic indexes of both ibuprofen and aspirin.

AN 141:400871 CA

TI **Anti-inflammatory** pharmaceutical compositions for reducing inflammation and the treatment or prevention of gastric toxicity

IN Babish, John G.; Tripp, Matthew L.; Bland, Jeffrey S.; Howell, Terrence; Darland, Gary K.; Lerman, Robert H.; Lukaczer, Daniel O.

PA USA

SO U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 689,856.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004219240	A1	20041104	US 2004-774048	20040205
	US 2003008021	A1	20030109	US 2001-885721	20010620
	US 2004086580	A1	20040506	US 2003-464410	20030618
	US 2004115290	A1	20040617	US 2003-464834	20030618

US 2004151792 A1 20040805 US 2003-689856 20031020
WO 2005039483 A2 20050506 WO 2004-US16043 20040521
WO 2005039483 A3 20050929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2001-885721 A2 20010620
US 2002-420383P P 20021021
US 2003-450237P P 20030225
US 2003-400293 B2 20030326
US 2003-401283 B2 20030326
US 2003-472460P P 20030522
US 2003-464410 A2 20030618
US 2003-464834 A2 20030618
US 2003-689856 A2 20031020
US 2004-774048 A 20040205
OS MARPAT 141:400871

L3 ANSWER 4 OF 8 CA COPYRIGHT 2005 ACS on STN
AB Compns. are provided including a synergistic combination of hops **isoalpha acids** and one or more isoflavones selected from genistein, genistin, daidzein, daidzin, glycitein and glycitin, wherein the weight ratio of hops **isoalpha acid** extract to isoflavones is from 1:50 to 50:1, calculated as aglycon. These compns. can be used as an **anti-inflammatory** agent or as a skin agent in particular for anti-ageing purposes. Examples given include Hops **isoalpha acids** increase procollagen and decorin synthesis in skin cells and the acids act synergistically to inhibit prostaglandin E2 expression in skin fibroblasts in response to stress.
AN 141:271563 CA
TI Hops **isoalpha acids** and isoflavones for **anti -inflammatory** and anti-ageing compositions
IN Yates, Paula Rachel
PA Unilever PLC, UK; Unilever NV; Hindustan Lever Limited
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004082697	A1	20040930	WO 2004-EP1785	20040224

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI GB 2003-6568 A 20030321
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 8 CA COPYRIGHT 2005 ACS on STN
AB Disclosed is a novel **anti-inflammatory** pharmaceutical composition that exhibits potent and selective inhibition of the cyclooxygenase-2 (COX-2) enzyme. The formulation consists of a hops extract

that exhibits COX-2 selectivity as defined by dividing the IC50 COX-2/IC50COX-1 concns. that are determined by testing with the William Harvey Whole Blood Assay (WHMA), and fall in the range 0.011-0.2. Such compns. may also optionally contain high levels of α-acids and low levels of β-acids, some flavonoid compds., and virtually no essential oils. Such compns. are useful for treating conditions that manifest as inflammatory **pain**, or are impacted by the COX-2 enzyme. The compns. are particularly beneficial for treating osteoarthritis and rheumatoid arthritis, and can be used for chronic **pain** with reduced gastric side-effects. A hops extract contained α-acids 88, β-acids 3.2, and **iso-.alpha. acids** 3%. The hops extract was more potent and selective than ibuprofen for inhibition of COX-2.

AN 141:111612 CA

TI Hop extracts as **anti-inflammatory** cyclooxygenase-2-selective inhibitors

IN Kuhrts, Eric H.

PA USA

SO U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004137096	A1	20040715	US 2003-340183	20030109
WO 2004062611	A2	20040729	WO 2004-US613	20040109
WO 2004062611	A3	20050407		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRAI US 2003-340183 A 20030109

L3 ANSWER 6 OF 8 CA COPYRIGHT 2005 ACS on STN

AB Disclosed is a pharmaceutical composition including a therapeutic quantity of a COX-2 inhibitor having an IC50-WHMA COX-2/COX-1 ratio ranging from about 0.23 to about 3.33 with reduced gastrointestinal and cardiovascular toxicity. Also disclosed are methods for treating osteoarthritis, rheumatoid arthritis or acute **pain** with less side-effects and faster onset of action utilizing the disclosed pharmaceutical composition A soft gelatin capsule was prepared by mixing a 70 % **iso-. alpha. acid** extract of hops with glycerin and other suitable excipients.

AN 138:374184 CA

TI Novel **anti-inflammatory** cyclooxygenase inhibitors having decreased gastrointestinal and cardiovascular toxicity

IN Kuhrts, Eric Hauser

PA USA

SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003091656	A1	20030515	US 2001-8778	20011113

PRAI US 2001-8778 20011113

L3 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AB Objective: Research suggests that osteoporosis is associated with systemic inflammation. We have previously shown that a reduced **iso-alpha acids** (RIAA), rosemary extract, and oleanolic acid supplement has **anti-inflammatory** effects by inhibiting COX-2-induced PGE2. We evaluated the anti-resorptive effects of this

supplement in osteoarthritis (OA) patients. Methods: An 8-week open-label pilot trial with the proprietary supplement in OA patients. Second morning urine was collected at initiation and conclusion. Bone resorption was measured using the collagen N-telopeptide (NTX) assay. Urinary NTX was converted to logarithm data to insure normal distribution and a 2-way ANOVA with interaction was performed. Tukey and Kramer&39;s test for honestly significant difference was performed post hoc. Results: 37 OA patients started the trial and 32 completed: 9 males (average age 53.6), 23 females (average age 50.7). A statistically significant ($p<0.005$) decrease in NTX was observed from the initial elevation of 66.9 +/- 7.96 (se) nmol BCE/mM to 38.2 +/- 3.39 nmol BCE/mM after 8 weeks on the supplement. Conclusions: This observation suggests that the proprietary RIAA, rosemary extract, and oleanolic acid supplement with **anti-inflammatory** properties may be useful in improving bone mineral density. Further controlled trials are planned.Research was funded by Metagenics, Inc.

AN 2004:292219 BIOSIS
DN PREV200400291701
TI Assessment of bone resorption in osteoarthritic subjects using a proprietary reduced **iso-alpha acids**, rosemary extract, and oleanolic acid supplement.
AU Lerman, Robert H [Reprint Author]; Lukaczer, Dan O; Darland, Gary K; Liska, DeAnn J; Schiltz, Barbara C; Tripp, Matthew L; Bland, Jeffrey S
CS Functional Medicine Research Center, Metagenics Inc., 9770 44th Ave NW, Gig Harbor, WA, 98332, USA
boblerman@metagenics.com
SO FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 608.3. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB. ISSN: 0892-6638 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jun 2004
Last Updated on STN: 23 Jun 2004

L3 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AB Objective: We have shown that a supplement of reduced **iso-alpha acids** (RIAA), rosemary extract, and oleanolic acid inhibits COX-2-specific PGE2 production in vitro. We assessed this supplement for effects on Osteoarthritis (OA), Rheumatoid Arthritis (RA), and Fibromyalgia (FM) in an open-label, 8 week trial. Methods: Supplement dose was 3 tabs/day for 4 weeks, which was continued or increased (4 tabs/day) for the subsequent 4 weeks, depending upon clinical response. **Pain** and quality-of-life were assessed using the Visual Analog Scale (VAS) and MOS Short-Form 36 (SF-36), respectively. Condition-specific data included the abridged Arthritis Impact Measurement Scale (AIMS2) for OA and RA, and the Fibromyalgia Impact Questionnaire (FIQ) for FM. Results: 62 subjects entered and 54 completed: 11 males (34-65 y), 43 females (28-68 y). Thirty-two subjects had OA, 19 FM, and 3 RA. OA subjects showed a 50% decrease in **pain** by VAS ($p<0.0001$; Wilcoxon-ranked sums) after supplementation. This decrease in **pain** was consistently observed in the AIMS2 and SF-36 **pain** subscale. No significant change in **pain** was seen for FM. Although **pain** decreased in RA, too few subjects precluded conclusions. Conclusions: The consistent findings of decreased **pain** specific for OA suggest that the RIAA, rosemary, and oleanolic acid supplement is the primary factor in **pain** improvement. Research supported by Metagenics. Inc. .
AN 2004:292123 BIOSIS
DN PREV200400291605
TI Benefits of a proprietary reduced **iso-alpha acids** (hops), rosemary extract, and oleanolic acid supplement on **pain** in subjects with osteoarthritis.
AU Lukaczer, Dan O [Reprint Author]; Lerman, Robert H; Darland, Gary K; Liska, DeAnn J; Schiltz, Barbara C; Tripp, Matthew L; Bland, Jeffrey S
CS Functional Medicine Research Center, Metagenics Inc., 9770 44th Ave NW,

Gig Harbor, WA, 98332, USA
danlukaczer@metagenics.com
SO FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 354.10.
http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jun 2004
Last Updated on STN: 23 Jun 2004